# SYNOPSIS

## 1. TITLE OF THE THESIS

**Oxidative degradation of antibiotics / analgesic drugs by colloidal $MnO_2$ in the absence and presence of micellar system**

## 2. INTRODUCTION

In recent years, the presence of pharmaceuticals in aquatic environment is a matter of great concern. Persistence against biological degradation and their biological activity are key properties of these pollutants. There has been an increasing concern about the pharmaceuticals in the aquatic environment [1]. The ubiquitous occurrence of antibiotics in aquatic environment raises concern about potential adverse effect on aquatic ecosystem and human health [2]. Pharmaceuticals are considered to be an emerging environment problem due to their continuous input and persistence to aquatic ecosystem even at low concentration [3]. Pharmaceutically active compounds are designed to act upon the function of living organism.

Many pharmaceuticals are present in aquatic environment. The quinolones are the family of synthetic broad-spectrum antibacterial drugs. The majority of quinolones in clinical use belong to the subset fluoroquinolones**.** Fluoroquinolones are the group of synthetic antimicrobial agents that play an important role in treatment of respiratory and bacterial infections [4]. The health concern regarding fluoroquinolones is based on their potential to promote antibiotic resistant bacteria but also on the possible toxic effects on microbial activity in wastewater treatment plants [5, 6]. Norfloxacin is the first antimicrobial agent belong to fluoroquinolone group. It is one of the most frequently detected antibiotic in wastewater effluents. It is also a synthetic broad spectrum chemotherapeutic antibacterial drug mainly used for the treatment of urinary tract infection. Its concentration range varies from 27 to 489 ng $L^{-1}$ [7-10]. Ciprofloxacin (CIP) is a second-generation fluoroquinolone antibiotic. It is famous for synthetic chemotherapeutic [4, 11]. Ciprofloxacin and norfloxacin are active against Gram positive and Gram negative bacteria. Ciprofloxacin is used to treat different types of bacterial infections. Chloramphenicol is also known as chlornitromycin, it is a bacteriostatic antimicrobial with wide range of clinical application for systemic and topical uses [12, 13]. Chloramphenicol is effective against a wide variety of Gram-positive and Gram-negative bacteria, including most anaerobic organisms. The most adverse effect with

chloramphenicol treatment is bone marrow toxicity, its function by inhibiting bacterial protein synthesis. Paracetamol is an antipyretic and analgesic compound of high therapeutic value [14-18]. Paracetamol is classified as a mild analgesic. paracetamol toxicity is one of the most common causes of poisoning worldwide. It is commonly used for the relief headache and pain.

Colloidal $MnO_2$ is one of the most active and important oxidative component which shows high potency in degrading various organic pollutants. Water soluble colloidal $MnO_2$ used as oxidant. Colloidal $MnO_2$ prepared in laboratory with appropriate concentration according to Perez-Benito et al. [19-21] the dark pink colored solution of $KMnO_4$ change to brown colored with the addition of $Na_2S_2O_3$. The $MnO_2$ is insoluble and form colloids with a typical diameter near 1 micron. In spite of wide ranging of application of $MnO_2$ as catalyst and oxidant its application are limited due to difficulties in solubility under ordinary conditions [22]. Antibiotic degradation mediated by manganese minerals is an important transformational process of antibiotics in aquatic environment [23]. Reaction between colloidal $MnO_2$ and organic reductants, play a key role in the redox cycling of manganese in the environment can be accelerated or inhibited.

The surfactants are surface active agent which signifícantly decrease the surface tension of water at relatively low concentration. Surfactants are amphipathic or amphiphilic molecules consist of two parts, namely apolar hydrophilic head group (water loving) and an apolar hydrophobic (water hating) tail (hydrocarbon chain). There are two characteristic feature of surfactants, surface activity and the ability to form micelles in solution, which affect the performance of surfactants [24]. Micellar induced reaction, due to their unique functional similarities with catalyzed reaction, have established an important place not only in chemical science but also in biochemical science [25]. Micellar pseudo-phase has been regarded as a microenvironment having varying degrees of polarity, water activity and hydrophobicity with increasing distance from the interfacial region to its core [26]. Surfactants are widely used in a variety of industrial and commercial application. Surfactants, showed their diverse application, as emulsifiers, wetting agents, solubilizers and preservatives are being exploited in domestic as well as industrial purpose ranging from soap to pharmaceuticals. Surfactants are used in pharmaceutical formulations not only as a tool to enhance drug solubility but also to increase their stability and reduce their side effects [27]. Both synthetic and biological surfactants have been used for this purpose. The proposed work

will be studied by micellar catalyst like CTAB (cetyltrimethyl ammonium bromide), SDS (Sodium dodecyl sulphate), Triton X-100, Polyethylene oxide group, Tetradyl-1-4-bis (cetyltrimethyl ammonium bromide), Cetyl pyridinium bromide and Brij 35 in the degradation of antibiotic and analgesic drugs in aquatic environment. The adsorption of surfactant at the solid–liquid interface plays an important role in many technological and industrial application.

## 3. A BRIEF REVIEW OF THE WORK ALREADY DONE IN THE FIELD

Lui et al. [4] addressed the formation and properties of degradation products of ciprofloxacin, norfloxacin and lomefloxacin during ozonation of secondary wastewater effluent. Hiremath et al. [13] has been investigated the kinetic oxidation of chloramphenicol by 1-chlorobenzotriazole (CBT) in $HClO_4$ medium over the temperature range 293–323 K. Singh et al. [14] investigated Pd(II) catalyzed oxidation of paracetamol (PA) by sodium N-chloro p-toluene sulfonamide in $HClO_4$ and NaOH solutions at 303 K. Singh et al. [18] has also been studied the mechanistic of iridium(III)-catalyzed oxidation of paracetamol by chloramine-T in aqueous perchloric acid medium at 308 K. Chen et al. [23] investigated by the a biotic transformation kinetics of chlortetracycline (CTC) by synthesized δ-$MnO_2$ under conditions of different solutions. CTC was rapidly oxidized by δ-$MnO_2$ with the generation of $Mn^{2+}$. Akram et al. [25] studied the kinetic oxidative degradation of peptide glycyl-glycine (Gly-Gly) by water-soluble colloidal $MnO_2$ in acidic medium in the aqueous and micellar media at 35°C. Nanda et al. [28] studied the kinetic oxidation of Norfloxacin by chloramine-B and N-chlorobenzotriazole by in aqueous acetic acid medium in the presence of perchloric acid at 323 K temperature. Kabir-ud-Din et al. [29] also reported kinetic oxidation of DL-mailic acid by water soluble colloidal $MnO_2$ spectrophotometically in the absence and presence of non-ionic Triton X-100 surfactant. Liu et al. [30] reported that sulfadiazine can be oxidatively degraded and even mineralized by manganese dioxide. Akram et al. [31] investigated the kinetic reduction of water-soluble colloidal manganese dioxide by glycyl-leucine (Gly-Leu) in presence of perchloric acid both in aqueous as well as micellar media at 35 °C. Watkinsona et al. [32] observed that the removal of 28 human and veterinary antibiotics in a conventional (activated sludge) and advanced (microfiltration/reverse osmosis) wastewater treatment plant. Chatzitakis et al. [33] reported the photo catalytic degradation of chloramphenicol, an antibiotic drug, in aqueous heterogeneous solution containing n-type

oxide semiconductors as photo catalysts. Wanga et al. [34] reported, the reaction kinetics and transformation of seven FQs ciprofloxacin (CIP), enrofloxacin (ENR), norfloxacin (NOR), ofloxacin (OFL), lomefloxacin (LOM), pipemidic acid (PIP) and flumequine (FLU)) and three structurally related amines (1-phenylpiperazine (PP), N phenylmorpholine (PM) and 4-phenylpiperidine (PD)) toward chlorine dioxide ($ClO_2$) elucidate the behavior of FQs during $ClO_2$ disinfection processes. Ilyas et al. [35] examined kinetic oxidation of l-methionine by colloidal $MnO_2$ in perchloric acid medium spectrophotometrically. Chirkst et al. [36] studied the kinetics of oxidation of phenol with manganese dioxide at pH 5.5 ± 0.5. Wanga et al. [37] reported the potential reactions of tetracycline's (TCs) with common water disinfection oxidants such as chlorine dioxide ($ClO_2$) and free- available chlorine (FAC). Altaf et al. [38] examined water soluble colloidal $MnO_2$ has been used to oxidize L-tyrosine in aqueous acidic medium in the absence and presence of non-ionic surfactant (TritonX-100) using a spectrophotometric technique. Tikahria et al. [39] studied the micellization behavior of cationic gemini surfactant, $C_{16}H_{33}N^+(CH_3)_2$-$(CH_2)_4$-$N^+(CH_3)_2C_{16}H_{33}$. $2Br^-$, in binary aqueous mixtures of dimethyl sulfoxide, methanol, 1, 4-dioxane, dimethyl formamide and ethylene glycol by conductivity measurement at 300-320 K. Singh et al. [40] reported the kinetics and mechanism of Ru(III)-catalyzed oxidation of paracetamolby chloramine-T (CAT) in aqueous perchloric acid medium at 303 K. Budri et al. [41] studied the kinetic of osmium(VIII) catalyzed oxidation of antibiotic drug chloramphenicol by hexacyanoferrate(III) in aqueous alkaline medium spectrophotometrically at 25°C. Babic et al. [42] were investigated the photolytic degradation of norfloxacin, enrofloxacin and ciprofloxacin, fluoroquinolone antibacterials widely used in human and veterinary medicine, under simulated solar irradiation in different water matrices. Katre et al. [43] reported the kinetic of oxidation of L-arginine by N-bromophthalamide in the presence of $HClO_4$ in different media, aqueous and micellar media of CTAB and SDS. Rajkumar et al. [44] have been attempted the oxidation of α-amino acids by permonosulphuric acid (PMS) at 27 ± 0.2°C in micellar medium.

## 4. OBJECTIVES

Our research work is to focus on the oxidative degradation of antibiotic / analgesic drugs and its mechanistic studies in aqueous and micellar system. The kinetic studies of oxidative degradation of antibiotics using colloidal $MnO_2$ in the absence and presence of micelle catalyst will be carried out with the experimental determination of reaction rate.

The main objectives of the present study are as follows:

i. To determine the order of reaction with respect to oxidant and substrate.
ii. Assessment the effect of $[H^+]$ / $[OH^-]$ on reaction rates.
iii. To see the effect of variation of surfactant concentration on reaction rates and critical micellar concentration (CMC).
iv. To study the effect of change of dielectric constant of the medium on the reaction rate.
v. To study the effect of ionic strength on the reaction rate.
vi. To study the stoichiometry and oxidation product of the reaction.
vii. To study the effect of temperature on the reaction rate and to calculate the thermodynamic activation parameters.
viii. To elucidate the reaction mechanism and to derive rate law from the observed kinetic results.
ix. Different model's will be used to explain the micellar behavior of the reaction.
x. Attempt will also be made for pharmaceutical effluent samples depends upon feasibility of the reaction.

## 5. NOTEWORTHY CONTRIBUTION IN THE FIELD OF PROPOSED WORK

In the aquatic environment the amount of pharmaceuticals is low. Its continuous input may constitute in the long term a potential risk for aquatic and terrestrial organism. The proposed study will help the scientific community to develop better understanding about complicated biochemical reactions in living things and aquatic environment. Present study deals with degradation of antibiotic / analgesic drugs by colloidal manganese dioxide in the absence and presence of micellar system. The phenomenon of micellar catalysis is the least subject of investigation in the field of chemical kinetics. Several workers [10, 15, 19, 40, 41] have been studied the degradation of drugs with various oxidant in the presence of surfactant / metal ion catalyst in acidic or alkaline medium.

## 6. PROPOSED METHODOLOGY

In the present work efforts will be made to develop suitable methods for oxidative degradation of drugs (antibiotics/analgesic) by colloidal $MnO_2$ in the absence and presence in

aqueous as well as micellar phase. Degradation of drugs will be monitored by decreasing the absorbance of unreacted colloidal manganese dioxide spectrophotometrically.

Kinetic study of above work will be carried out to establish the optimum condition to develop a simple procedure for oxidative degradation of drugs in aqueous as well as in micellar media. The oxidation product will be characterized by **TLC** / **FTIR** and **GC-MS** techniques.

The proposed plan of study will be as follows:

**a**. **Kinetic Studies:** For kinetic measurements, UV-Visible spectrophotometer or visible spectrophotometer will be used. The oxidation of drugs by colloidal $MnO_2$ will be done under pseudo-first order condition. The progress of reaction will be studied spectrophotometrically by monitoring the decrease in absorbance of unreacted oxidant in the reaction mixture. It will be verified that other constituents of the reaction mixture do not absorb significantly at this wavelength. The application of Beer Lambert's law will also be verified.

**b. Reaction Orders:** The order of reaction will be determine from the slope of log $k_{obs}$ versus log (concentration) plots by varying the concentration of reactant while keeping all other concentrations and conditions constant. The first order rate constant, $k_{obs}$ will be obtained from the plots of log absorbance versus time.

**c. Ostwald isolation method:** A method for determining the order of a reaction with respect to one reactant at a time. The basic principle is that when one reactant is taken in large excess compared to the other reactant, the change in concentration in the first reactant is negligible.

**d. Determination of CMC:** The CMC is the narrow range of concentration over which amphiphile solution show an abrupt change in physical properties. The CMC can be determined by the intersection of two straight lines of a variety of solution properties above and below the CMC. Concentration called critical micelle concentration (CMC) to form micelle. CMC will be determine from plots of the specific conductivity versus surfactant concentration. In the present work CMC will be determined by the use of surface tension / conductivity meter. The knowledge of the CMC is important for the calculation of the thermodynamic parameters degree of dissociation (α), Gibbs free energy ($\Delta G^{\#}$), enthalpy ($\Delta H^{\#}$), and entropy ($\Delta S^{\#}$) which will confirm the scientific interest of a precise determination of the CMC.

**e. Models apply:**

**i. Berezin's pseudo phase model**- Berezin and co-workers developed the first general treatment based on the pseudo phase model and successfully simulated spontaneous and bimolecular reactions between neutral and organic reactants. The inhibition of rates at higher concentration of surfactant may be explained with the help of Berezin's model, which involves solubilisation of both the reactant in the micellar phase. According to the Berezin's approach a solution above the critical micelle concentration (CMC) may be considered as a two-phase system, consisting of an aqueous phase and a micellar pseudo-phase.

**ii. Piszkiewicz's model** - Piszkiewicz's proposed a model for micellar catalyzed reaction analogous to the Hill model of enzyme kinetics. This model is applicable specially at low surfactant concentration.

**iii. Menger and Portnoy model** – Inhibition of micelles involves at least three main steps (1) binding of the substrate to micelle, (2) the actual chemical transformation in the micelle, and (3) release of product. Menger and Portnoy developed a pseudo phase model, which has been fitted to various micellar-catayzed reactions. According to this model the variation of the rate constant with surfactant is generally treated on the assumption that substrate (S) is distributed between the aqueous and micelle-phases.

**iv. Raghavan and shrinivasan's model –** For bimolecular micellar catalyzed reactions, Raghavan and shrinivasan developed a model. The distribution of the reactants in aqueous and micellar phase has been considered in the model. This model predicts constancy in $k_\psi$ values at high surfactant concentrations. The product formation is assumed to result from the decomposition of a ternary complex involving substrate, nucleophile, and micelle.

## 7. EXPECTED OUTCOME OF THE PROPOSED WORK

Proposed study investigated the removal and transformation of antibiotic / analgesic drugs by the use of eco-friendly oxidation colloidal $MnO_2$ in the absence and presence of micellar system.

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## 9. LIST OF PAPERS COMMUNICATED / SUBMITTED / PUBLISHED / IN JOURNALS CONFERENCE / SYMPOSIUM

### PAPER COMMUNICATED

"Mechanistic aspects of uncatalyzed and silver nanoparticles catalyzed oxidation of norfloxacin by water soluble colloidal manganese dioxide in aqueous alkaline medium: A comparative kinetic study".

### PAPER PRESENTED IN CONFERENCE

1. Paper presented on "kinetic study of uncatalyzed and catalyzed oxidation of norfloxacin by colloidal manganese dioxide".

National Seminar on "**Chemistry In Our Lives**" 1st & 2nd February, 2013. Organized by Department of Chemistry Govt. E. Raghvendra Rao P. G. Science College, Bilaspur (C. G.).

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